

Type	L #	Hits	Search Text	DBs	Time Stamp	Com ments	Err or Def ro ments
1	BRS	L2	467	TFPI	USPAT; US-PGPUB; EPO; 7 14:12 JPO; DERWENT	2003/04/2 7 14:12	0
2	BRS	L3	53	TFPI-2	USPAT; US-PGPUB; EPO; 7 14:12 JPO; DERWENT	2003/04/2 7 14:12	0
3	BRS	L4	64	TFPI same (mutat\$3 or mutein or substitut\$3)	USPAT; US-PGPUB; EPO; 7 14:13 JPO; DERWENT	2003/04/2 7 14:13	0
4	BRS	L5	26	TFPI-2 same (mutat\$3 or mutein or substitut\$3)	USPAT; US-PGPUB; EPO; 7 14:14 JPO; DERWENT	2003/04/2 7 14:14	0
5	BRS	L6	40252	chimeric or (fusion adj protein)	USPAT; US-PGPUB; EPO; 7 14:15 JPO; DERWENT	2003/04/2 7 14:15	0
6	BRS	L7	10	(2 or 4) same (3 or 5) same 6	USPAT; US-PGPUB; EPO; 7 14:16 JPO; DERWENT	2003/04/2 7 14:16	0
7	BRS	L8	370	heparin adj binding adj domain	USPAT; US-PGPUB; EPO; 7 14:18 JPO; DERWENT	2003/04/2 7 14:18	0
8	BRS	L9	380	protease adj nexin\$1	USPAT; US-PGPUB; EPO; 7 14:19 JPO; DERWENT	2003/04/2 7 14:19	0
9	BRS	L10	380	protease adj nexin\$2	USPAT; US-PGPUB; EPO; 7 14:19 JPO; DERWENT	2003/04/2 7 14:19	0
10	BRS	L11	2311	antithrombin adj III	USPAT; US-PGPUB; EPO; 7 14:24 JPO; DERWENT	2003/04/2 7 14:24	0
11	BRS	L12	365	heparin adj cofactor adj II	USPAT; US-PGPUB; EPO; 7 14:24 JPO; DERWENT	2003/04/2 7 14:24	0

Type	L #	Hits	Search Text	DBs	Time Stamp	Com ments	Err or Def iners
12	BRS	L13	protein adj c adj inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/2 7 14:24		0
13	BRS	L14	platelet adj factor\$14	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/2 7 14:24		0
14	BRS	L15	bovine adj pancreatic adj trypsin adj inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/2 7 14:25		0
15	BRS	L16	ghilanten\$1related adj inhibitor	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/2 7 14:25		0
16	BRS	L17	(heparin adj binding adj domain) same ((protease adj nexin\$1) or (protease adj nexin\$12) or (antithrombin adj III) or (heparin adj cofactor adj II) or (protein adj c adj inhibitor) or (platelet adj factor\$14) or (bovine adj pancreatic adj trypsin adj inhibitor) or (ghilanten\$1related adj inhibitor ))	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/2 7 14:27		0
17	BRS	L18	0 same 17	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/2 7 14:28		0

Type	L #	Hits	Search Text	DBs	Time Stamp	Com ments	Err or Def inits	Er rors
18	BRS	L19	45 innis adj michael.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/2 7 14:28		0	
19	BRS	L20	23 creasey adj abla.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/2 7 14:28		0	
20	BRS	L21	5 (19 or 20) and 7	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/04/2 7 14:29		0	

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ENTRY SESSION  
FULL ESTIMATED COST 0.21 0.21

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FILE 'AGRICOLA' ENTERED AT 14:32:17 ON 27 APR 2003

```
=> s TFPI
L1          3493 TFPI

=> s TFPI-2
L2          229 TFPI-2

=> s (chimeric protein) or (fusion protein)
  5 FILES SEARCHED...
L3          160224 (CHIMERIC PROTEIN) OR (FUSION PROTEIN)

=> s L1 (p) l2 (p) l3
L4          3 L1 (P) L2 (P) L3

=> duplicate remove l4
DUPLICATE PREFERENCE IS 'CAPLUS, BIOSIS'
KEEP DUPLICATES FROM MORE THAN ONE FILE?  Y/ (N) :n
PROCESSING COMPLETED FOR L4
L5          3 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)
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=> d 15 1-3 ibib abs

L5 ANSWER 1 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
ACCESSION NUMBER: 2001:340475 BIOSIS  
DOCUMENT NUMBER: PREV200100340475  
TITLE: Chimeric proteins.  
AUTHOR(S): Innis, Michael A.; Creasey, Abla A.  
ASSIGNEE: Chiron Corporation  
PATENT INFORMATION: US 6174721 January 16, 2001  
SOURCE: Official Gazette of the United States Patent and Trademark  
Office Patents, (Jan. 16, 2001) Vol. 1242, No. 3, pp. No  
Pagination. e-file.  
ISSN: 0098-1133.  
DOCUMENT TYPE: Patent  
LANGUAGE: English  
AB \*\*\*Chimeric\*\*\* \*\*\*proteins\*\*\* possessing Kunitz-type domain 1 of  
\*\*\*TFPI\*\*\* - \*\*\*2\*\*\* and Kunitz-type domain 2 of \*\*\*TFPI\*\*\* are  
disclosed, as are muteins of \*\*\*TFPI\*\*\* and \*\*\*TFPI\*\*\* - \*\*\*2\*\*\*  
. Nucleic acid sequences, expression vectors and transformed host cells  
encoding and capable of producing the disclosed \*\*\*chimeric\*\*\*  
\*\*\*proteins\*\*\* and muteins are also disclosed. Finally, methods for  
prevention and treatment of septic shock using the \*\*\*chimeric\*\*\*  
\*\*\*proteins\*\*\* and muteins are disclosed.

1.5 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1996:2950 CAPLUS  
 DOCUMENT NUMBER: 124:3253  
 TITLE: \*\*\*Chimeric\*\*\* \*\*\*proteins\*\*\* and muteins of  
 tissue factor pathway inhibitors \*\*\*TFPI\*\*\* and  
 \*\*\*TFPI\*\*\* - \*\*\*2\*\*\*  
 INVENTOR(S): Innis, Michael A.; Creasey, Alba A.  
 PATENT ASSIGNEE(S): Chiron Corporation, USA  
 SOURCE: PCT Int. Appl., 67 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9604378	A2	19960215	WO 1995-US9464	19950725
WO 9604378	A3	19960314		
W: AU, CA, JP, MX				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
US 5589359	A	19961231	US 1994-286521	19940805
US 5563123	A	19961008	US 1995-437841	19950509
US 5696088	A	19971209	US 1995-436175	19950509
CA 2196290	AA	19960215	CA 1995-2196290	19950725
AU 9531500	A1	19960304	AU 1995-31500	19950725
AU 710535	B2	19990923		
EP 776366	A1	19970604	EP 1995-927478	19950725
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE				
JP 10503375	T2	19980331	JP 1996-506598	19950725
US 6174721	B1	20010116	US 1997-943682	19971014
US 2002197667	A1	20021226	US 2000-741106	20001221
PRIORITY APPLN. INFO.:				
			US 1994-286521	A 19940805
			US 1995-438184	B1 19950509
			WO 1995-US9464	W 19950725
			US 1997-943682	A1 19971014

AB \*\*\*Chimeric\*\*\* \*\*\*proteins\*\*\* possessing Kunitz-type domain 1 or  
 \*\*\*TFPI\*\*\* - \*\*\*2\*\*\* and Kunitz-type domain 2 of \*\*\*TFPI\*\*\* are  
 provided, as are muteins of \*\*\*TFPI\*\*\* and \*\*\*TFPI\*\*\* - \*\*\*2\*\*\*.  
 Nucleic acid sequences, expression vectors, and transformed host cells  
 encoding and capable of producing the disclosed \*\*\*chimeric\*\*\*  
 \*\*\*proteins\*\*\* and muteins are also provided. \*\*\*Chimeric\*\*\*  
 \*\*\*proteins\*\*\* were constructed with amino acid sequences capable of  
 binding a cell surface component (glycosaminoglycan, heparin) such as  
 peptide moieties from protease nexin-1, protease nexin-2, antithrombin  
 III, heparin cofactor II, protein C inhibitor, platelet factor 4, bovine  
 pancreatic trypsin inhibitor, and ghilanten-related inhibitors. The  
 \*\*\*chimeric\*\*\* \*\*\*proteins\*\*\* are produced as yeast .alpha.-factor  
 \*\*\*fusion\*\*\* \*\*\*proteins\*\*\* for secretion, or alternatively, may be  
 expressed as a ubiquitin \*\*\*fusion\*\*\* \*\*\*protein\*\*\*. Potential  
 sites for N-like glycosylation within \*\*\*TFPI\*\*\* (Asn116.fwdarw.Gln,  
 Asn227.fwdarw.Gln) are removed using overlapping PCR and mutations och1,  
 mn1, and alg3 are introduced in transformed yeast cells to prevent the  
 prodn. of .alpha.-1,6-polymannose terminal carbohydrate moieties in the  
 chimeric products. Finally, methods for prevention and treatment of  
 septic shock using the \*\*\*chimeric\*\*\* \*\*\*proteins\*\*\* and muteins  
 are described.

L5 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2003 ACS  
 ACCESSION NUMBER: 1996:302444 CAPLUS  
 DOCUMENT NUMBER: 124:334850  
 TITLE: Production of homogeneous, biologically active tissue  
 factor pathway inhibitor with yeast  
 INVENTOR(S): Innis, Michael A.; Creasey, Alba A.  
 PATENT ASSIGNEE(S): Chiron Corporation, USA  
 SOURCE: PCT Int. Appl., 36 pp.  
 CODEN: PIXXD2  
 DOCUMENT TYPE: Patent  
 LANGUAGE: English  
 FAMILY ACC. NUM. COUNT: 1  
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
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WO 9604377 A1 19960225

WO 1995-US9377 19950

W: AU, CA, JP, MX

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

CA 2196296 AA 19960215 CA 1995-2196296 19950725

AU 9531044 A1 19960304 AU 1995-31044 19950725

AU 707762 B2 19990722

EP 774001 A1 19970521 EP 1995-926779 19950725

EP 774001 B1 20021016

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, MC, NL, PT, SE

JP 10507071 T2 19980714 JP 1995-506588 19950725

AT 226249 E 20021115 AT 1995-926779 19950725

US 6103500 A 20000815 US 1997-854764 19970512

PRIORITY APPLN. INFO.: US 1994-286530 A 19940805

WO 1995-US9377 W 19950725

AB A method for the prodn. of Tissue Factor Pathway Inhibitor ( \*\*\*TFPI\*\*\* ) and Tissue Factor Pathway Inhibitor 2 ( \*\*\*TFPI\*\*\* - \*\*\*2\*\*\* ) and muteins thereof is disclosed wherein the protein is retained within a yeast cell during growth of the yeast cell and recovered from an insol. fraction prep'd. from yeast cells contg. the protein. This method produces full-length, homogeneous TFP having the correct N-terminal amino acid sequence. Plasmid pLACI 4.1, which contains a chimeric gene encoding a ubiquitin-mature TFP1 \*\*\*fusion\*\*\* \*\*\*protein\*\*\*, was prep'd. S. cerevisiae strains VH6, AB122, and JSC310 transformed with this plasmid produced TFP1 at 5,10, and 15% of total protein, resp. The TFP1 was biol. active.

=> s heparin binding domain

L6 2995 HEPARIN BINDING DOMAIN

=> s (protease nexin 1) or (protease nexin 2) or (antithrombin III) or (heparin cofactor II) or (4 FILES SEARCHED...)

L7 47084 (PROTEASE NEXIN 1) OR (PROTEASE NEXIN 2) OR (ANTITHROMBIN III)  
OR (HEPARIN COFACTOR II) OR (PROTEIN C INHIBITOR) OR (PLATELET  
FACTOR 4)

=> s (bovine pancreatic trypsin inhibitor) or (ghilanten-related inhibitor)

L8 3568 (BOVINE PANCREATIC TRYPSIN INHIBITOR) OR (GHILANTEN-RELATED  
INHIBITOR)

=> s 16 (p) (17 or 18)

L9 159 L6 (P) (L7 OR L8)

=> d his

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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
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L1 3493 S TFPI

L2 229 S TFPI-2

L3 160224 S (CHIMERIC PROTEIN) OR (FUSION PROTEIN)

L4 3 S L1 (P) L2 (P) L3

L5 3 DUPLICATE REMOVE L4 (0 DUPLICATES REMOVED)

L6 2995 S HEPARIN BINDING DOMAIN

L7 47084 S (PROTEASE NEXIN 1) OR (PROTEASE NEXIN 2) OR (ANTITHROMBIN II

L8 3568 S (BOVINE PANCREATIC TRYPSIN INHIBITOR) OR (GHILANTEN-RELATED I

L9 159 S L6 (P) (L7 OR L8)

=> s 14 (p) 19

L10 0 L4 (P) L9

=> d his

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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
14:32:17 ON 27 APR 2003

L1 3493 S TFPI

L2 229 S TFPI-2

L3 160224 S (CHIMERIC PROTEIN) OR (FUSION PROTEIN)

L4 3 S L1 (P) L2 (P)  
L5 3 DUPLICATE REMOVE (0 DUPLICATES REMOVED)  
L6 2995 S HEPARIN BINDING DOMAIN  
L7 47084 S (PROTEASE NEXIN 1) OR (PROTEASE NEXIN 2) OR (ANTITHROMBIN II  
L8 3568 S (BOVINE PANCREATIC TRYPSIN INHIBITOR) OR (GHILANTEN-RELATED I  
L9 159 S L6 (P) (L7 OR L8)  
L10 0 S L4 (P) L9

=> log y

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FULL ESTIMATED COST	76.04	76.25
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CA SUBSCRIBER PRICE	-1.30	-1.30

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